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EDITORIAL COMMENT

Culprit Plaque in Myocardial Infarction

Going Beyond Angiography*

Aloke V. Finn, MD,† Gaku Nakazawa, MD,‡
Jagat Narula, MD, PhD, FACC,§
Renu Virmani, MD, FACC‡

Atlanta, Georgia; Gaithersburg, Maryland; and Irvine, California

Coronary angiographic studies conducted over 20 years ago helped confirm thrombosis as the cause of acute myocardial infarction (AMI) (1). However, with the emerging newer technologies, the limitations of conventional angiography for furthering our understanding of the pathophysiology of AMI are becoming apparent. Although angiography does help to visualize the location of flow obstruction, its usefulness in identifying the exact location and characteristics of culprit plaque is limited. In cases of total luminal occlusion, the site of the culprit plaque is undetectable.

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From pathologic studies conducted in patients dying of coronary heart disease, it is well known that plaque rupture is the dominant cause of luminal thrombosis, which might propagate upstream or downstream from the culprit site (2); plaque rupture is responsible for 60% to 70% of acute coronary events. Plaque erosion is another significant but less frequent cause of AMI and sudden death, occuring in 25% to 40% of cases (2,3). What distinguishes lesions with rupture from other plaques in the coronary tree is a thin and inflamed fibrous cap that overlies a large necrotic core (4). However, detecting plaques on the basis of such characteristics is not easily feasible in living patients. The development of imaging modalities, including intravascular ultrasound (IVUS) and optical coherence tomography, has been proposed to identify morphologic attributes of unstable plaques (5–7). However, intravascular coronary thermography (8) has allowed assessment of the functional component of the plaque by demonstrating temperature elevation in culprit plaques in patients presenting with AMI; the increase in temperature occurs presumably because of heat released by activated inflammatory cells (9–11).

In this issue of the *Journal*, Takumi et al. (12) demonstrate the utility of thermography and the limitations of conventional angiography for detecting the site of the culprit plaque in 45 consecutive patients presenting with anterior AMI. They report that the maximal temperature (Tmax) site was significantly more distal to the angiographically most stenotic site in patients presenting with either total occlusion or reperfusion, although the relationship was far stronger for those with occlusion than reperfusion. In the subset of patients with reperfusion, the location of the culprit plaque by IVUS, angiography, and thermal wire was in closer proximity. In contrast, in those patients with occlusive lesions, the angiographically occlusive site was significantly more proximal to the culprit plaque as determined by IVUS and thermography. Although the authors emphasize that the colocalization of IVUS and Tmax at a mean distance of 9 mm distal from the site of occlusion ensures the accuracy of thermal wire for detecting the rupture site, they only document plaque rupture in 25% of patients; the lesion morphology underlying thrombi in the remaining 75% of patients with total occlusions remains unclear. Even in patients with reperfused lesions, where thrombus burden is presumably much less, the authors demonstrate the presence of plaque rupture in only 50% of patients with the rupture, and Tmax site was located 1 mm distal to the narrowest angiographic portion. An overall low plaque rupture rate of 37% might be related to the limited resolution of imaging techniques, or it is possible that luminal thrombi in the remaining 63% of lesions might have resulted from plaque erosion. It is unlikely that the erosive plaques would cause an increase in temperature, because inflammatory infiltration is much less common.

From these findings it seems clear that large amounts of thrombus generated in the setting of ST-segment elevation MI often propagates upstream, obscuring the culprit plaque (Fig. 1). The fact that there was a good correlation between the Tmax site and that of IVUS adds additional validation to the use of thermography for the detection of culprit plaques in vivo and suggests that modalities aimed at detecting temperature as a surrogate for inflammation might be useful for localizing the culprit plaque.

Although these results are encouraging, we must also be cautious about the limitations of this study. First, the validation of thermal wire technology was carried out in human carotid plaques in ex vivo. The experimental data have been generated in diet-induced atherosclerotic iliac arteries in rabbits, wherein the lesions are predominantly composed of foamy macrophages (13,14). These few studies do not necessarily translate into the in vivo accuracy of thermography for detection of inflamed plaques. The in vivo validation of thermal wire technology in this study was

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From the †Emory University School of Medicine, Atlanta, Georgia; ‡CVPath Institute, Inc., Gaithersburg, Maryland; and the §University of California, Irvine, California.

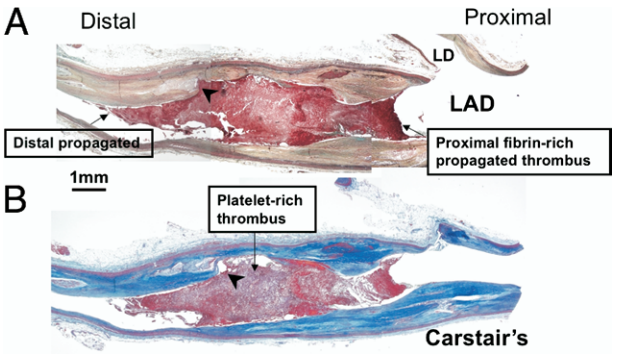

Figure 1 **Thrombus Propagation in Plaque Rupture**

(A) Composite of a longitudinal section of proximal left anterior descending (LAD) and left diagonal (LD) coronary arteries with plaque rupture in the LAD. Note propagation of the thrombus upstream from the site of plaque rupture **(arrowheads)** extending up to the first major sidebranch (LD). **(B)** The same longitudinal section with Carstair's stain for detection of fibrin **(dark red)** and platelets **(blue-gray)**. The proximal and distal propagated thrombus consists predominantly of fibrin and red cells, whereas the rupture site has platelet-rich thrombus. Modified with permission from Virmani et al., editors. The Vulnerable Plaque: Strategies for Diagnosis and Management. Malden, MA: Blackwell Publishing, 2007.

based upon correlation with IVUS, where a large lipid core or a ruptured cap was used to define the culprit plaque. Not all plaque ruptures have a large necrotic core, and IVUS could easily miss lesions that have a small necrotic core (Fig. 2). Moreover, as mentioned already, plaque rupture was detected in only 37% of patients undergoing IVUS study, far below the 70% found in pathologic studies of patients dying suddenly of coronary disease. These issues emphasize the need for better imaging modalities with higher resolution.

These concerns, however, should not diminish the importance of this study. What we should take away is that we are entering an age where technology and our imagination are allowing us to go beyond the confines of angiography. We are beginning to understand atherosclerotic plaques in vivo rather than from still histologic images obtained at autopsy. It is ultimately the plaque composition of the arterial wall in living patients rather than luminal thrombus burden that will start to free us from the limits of "lumenography."

Reprint requests and correspondence: Dr. Renu Virmani, Medical Director, CVPath Institute, Inc., 19 Firstfield Road, Gaithersburg, Maryland 20878. E-mail: rvirmani@cvpath.org.

REFERENCES

1. DeWood MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Med 1980;303:897–902.
2. Virmani R, Kolodgie FD, Burke AP, Farb A, Schwartz SM. Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions. Arterioscler Thromb Vasc Biol 2000;20:1262–75.
3. Arbustini E, Dal Bello B, Morbini P, et al. Plaque erosion is a major substrate for coronary thrombosis in acute myocardial infarction. Heart 1999;82:269–72.
4. Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable plaque. J Am Coll Cardiol 2006;47:C13–8.

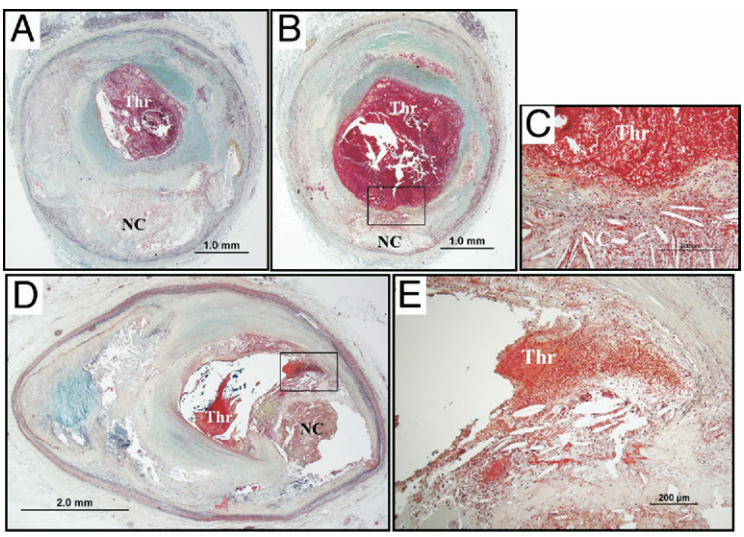

Figure 2 **Two Cases of Sudden Coronary Death**

(A) Proximal section shows severe narrowing of the lumen with a relatively large necrotic core area (NC) in the absence of plaque rupture, whereas the distal nonstenotic section **(B)** reveals the rupture site **(C)** with a much smaller NC and an occlusive thrombus (Thr). It is therefore possible that intravascular ultrasound would not be able to detect the distal site of rupture, because the NC is small. **(D and E)** Section of left anterior descending coronary artery at the site of severest luminal narrowing with a nonocclusive Thr. Note large NC with overlying ruptured thin fibrous cap **(box area)** and a higher magnification in **panel E**. Intravascular ultrasound would easily detect the large NC.

5. Mintz GS, Nissen SE, Anderson WD, et al. ACC clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound studies: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents (Committee to Develop a Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies [IVUS]). J Am Coll Cardiol 2001;37:1478–92.
6. Rodriguez-Granillo GA, Garcia-Garcia HM, Mc Fadden EP, et al. In vivo intravascular ultrasound-derived thin-cap fibroatheroma detection using ultrasound radiofrequency data analysis. J Am Coll Cardiol 2005;46:2038–42.
7. Yabushita H, Bouma BE, Houser SL, et al. Characterization of human atherosclerosis by optical coherence tomography. Circulation 2002;106:1640–5.
8. Stefanadis C, Diamantopoulos L, Vlachopoulos C, et al. Thermal heterogeneity within human atherosclerotic coronary arteries detected in vivo: a new method of detection by application of a special thermography catheter. Circulation 1999;99:1965–71.
9. Stefanadis C, Toutouzas K, Tsiamis E, et al. Increased local temperature in human coronary atherosclerotic plaques: an independent predictor of clinical outcome in patients undergoing a percutaneous coronary intervention. J Am Coll Cardiol 2001;37:1277–83.
10. Stefanadis C, Toutouzas K, Tsiamis E, et al. Thermal heterogeneity in stable human coronary atherosclerotic plaques is underestimated in vivo: the "cooling effect" of blood flow. J Am Coll Cardiol 2003;41:403–8.
11. Toutouzas K, Synetos A, Stefanadi E, et al. Correlation between morphologic characteristics and local temperature differences in culprit lesions of patients with symptomatic coronary artery disease. J Am Coll Cardiol 2007;49:2264–71.
12. Takumi T, Lee S, Hamasaki S, et al. Limitation of angiography to identify the culprit plaque in acute myocardial infarction with coronary total occlusion: utility of coronary plaque temperature measurement to identify the culprit plaque. J Am Coll Cardiol 2007;50:2197–203.
13. Casscells W, Hathorn B, David M, et al. Thermal detection of cellular infiltrates in living atherosclerotic plaques: possible implications for plaque rupture and thrombosis. Lancet 1996;347:1447–51.
14. Verheye S, De Meyer GR, Van Langenhove G, Knaapen MW, Kockx MM. In vivo temperature heterogeneity of atherosclerotic plaques is determined by plaque composition. Circulation 2002; 105:1596–601.